

mean dose comparisons (T-pair and Kruskal-Wallis tests), log rank tests on event-free survivals, and probit analyses. The highest graded event, or in cases of similar grade the earliest, was considered for analyses.

**Results:** One hundred and fifteen patients were eligible. Of them, 94.8% received concomitant chemoradiotherapy; 12.2% extended-field radiotherapy, and 32.2% nodal sequential boost. Their mean age was 47.5 years. The median follow-up was 35.5 months. A total of 522 events was reported. Focusing on the highest grade per patient: 17 had grade 0, 75, grade 1, 20, grade 2 and 3, grade 3. The prevalence of grade 1 events appeared stable during the study period, ranging between 31.2 and 50%. The one of grade 2 events tended to worsen: 2.2% at 6 months, 4.5% at 1 year, 6.9% at 2 years, and 7.0% at 3 years. Incidences of grade 2-4 events were 0.9% at 6 months, 6.6%, 19.0%, and 27.2% at 1, 2, 3 years respectively. The mean D2cm3 and D0.1cm3 were respectively  $68.7 \pm 13.6$  Gy and  $85.8 \pm 33.1$  Gy and did not differ according to grade ( $p=0.47$  and  $p=0.52$ ). Comparisons of mean D2cm3 and D0.1cm3 according to grade 0-1 versus 2-4 were not significant ( $68.0 \pm 12.4$  vs  $71.4 \pm 17.7$  Gy,  $p=0.38$  and  $83.7 \pm 26.4$  vs  $94.5 \pm 51.9$  Gy,  $p=0.33$  respectively). Log rank tests were performed after splitting patients into 4 groups according to D2cm3 levels:  $> 80$  Gy, 70 to 79 Gy, 60 to 70 Gy and  $< 60$  Gy. No difference was observed for grade 1-4 ( $p=0.52$ ), grade 2-4 ( $p=0.52$ ) or grade 3-4 ( $p=0.21$ ). Probit analyses showed no correlation between both dosimetric parameters and the probability of small bowel events grade 1-4, 2-4, or 3-4 ( $p$  ranging from 0.19 to 0.48).

**Conclusion:** No significant dose-volume effect relationships were demonstrated between the D2cm3 and D0.1cm3 and the probability of late small bowel morbidity. These two parameters should not limit the optimization process.

#### OC-0352

The high doses employed in brachytherapy of cervical cancer counteract hypoxia - a modelling study

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**Purpose or Objective:** Brachytherapy is a well-established radiotherapy treatment modality that has been employed in treatments of several cancer types for more than a century. One of the most common treatment strategies for cervical cancer today is a combination of external beam radiotherapy, chemotherapy and brachytherapy. Similar to other forms of radiation therapy, pre-treatment imaging of hypoxia is rarely done for cervical cancer. Nevertheless, the clinical outcome is highly positive, despite the fact that hypoxia has been repeatedly confirmed in cervical tumours. It was therefore the purpose of this study to investigate whether the success of brachytherapy in these tumours, seemingly regardless of oxygenation status, could be explained by the characteristics of the brachytherapy dose distributions in comparison to external beam radiotherapy.

**Material and Methods:** A previously used *in silico* model of tumour oxygenation and radiation response was further developed to simulate the treatment of cervical cancer employing the combination of external beam radiotherapy and intracavitary brachytherapy. Based on the local clinical protocol and using a clinically derived brachytherapy dose distribution and assuming a homogeneous dose delivered by external radiotherapy, survival was assessed on voxel level taking into account the dose-modifying effect of the oxygenation as well as the effects of repair and repopulation of tumour cells during treatment. Two scenarios were considered for brachytherapy: one in which the high dose region was highly conformal to the hypoxic region in the target and one in which they were displaced relative to each other. Overall-response was assessed as Poisson-based

tumour control probability (TCP). The interplay between tumour oxygenation and the heterogeneous high-dose distribution was also studied by simulating different spatial and temporal patterns of hypoxia. The results were compared to the case when irradiation was performed only with external beams delivering a homogeneous dose to the target.

**Results:** Predicted values of D50 with respect to the external treatment and assuming reoxygenation were in agreement with the clinically observed high cure rates. Assuming fast reoxygenation, the D50 was similar for the different cases of overlap between the brachytherapy dose distribution and the tumour, regardless if the hypoxic fraction was 10% or 25% (Table 1). To achieve 50% control with external RT only, a total dose of more than 70 Gy in 25 fractions would be required for both cases of hypoxic fraction assuming reoxygenation (Figure 1).

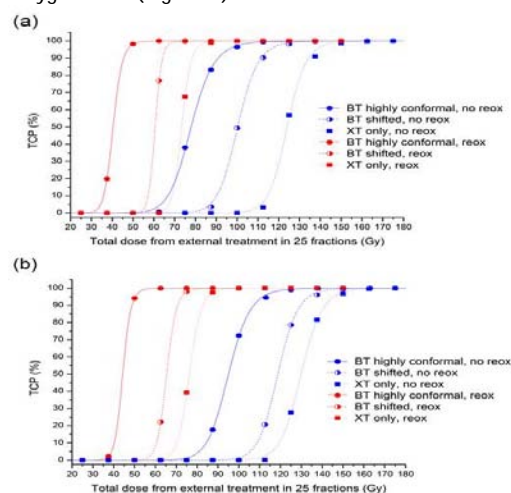


Figure 1. TCP curves for external RT given in 25 fractions for various scenarios for the brachytherapy (BT) dose distribution: highly conformal or shifted relative to the hypoxia area and the corresponding curves for the external RT (XT) only, for a simulated tumour with 10% hypoxia in (a) and 25% hypoxia in (b).

Hypoxic fraction	Oxygenation pattern	D <sub>50</sub> (Gy)		
		BT highly conformal	BT shifted	XT only
10%	No reoxygenation	77.9	100.3	124.1
	Fast reoxygenation	40.4	60.6	73.4
25%	No reoxygenation	95.1	118.7	129.9
	Fast reoxygenation	44.3	65.4	76.2

Table 1. Values of D<sub>50</sub> for external RT given in 25 fractions for various scenarios for the brachytherapy (BT) dose distribution: highly conformal or shifted relative to the hypoxia area and the corresponding values for the external RT (XT) only.

**Conclusion:** Assuming fast reoxygenation, the dependence on the degree and extent of hypoxia has little impact on the outcome and therefore the high doses delivered in brachytherapy could counteract the negative impact of hypoxia.

#### OC-0353

EBRT and interstitial brachytherapy for recurrent vault carcinomas: Factors influencing the outcomes

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**Purpose or Objective:** Post hysterectomy vaginal vault recurrences have poor outcomes with pelvic control rates ranging from 50-60%. We conducted this prospective study at our centre with an aim to determine the factors influencing